

**CLAIMS**

What is claimed is:

1. An antagonist that inhibits angiogenesis by modifying protein-protein interactions, wherein the protein-protein interactions comprise interactions between at least one amino acid sequence within a first protein and at least one amino acid sequence within a second protein.
2. The antagonist of claim 1 wherein the first protein is MMP-9.
3. The antagonist of claim 1 wherein the first protein is a  $\beta$ 1-containing integrin.
4. The antagonist of claim 1 wherein the first protein is MMP-9 and the second protein is a  $\beta$ 1-containing integrin.
5. The antagonist of claim 4 wherein the protein-protein interactions cause MMP-9 to bind to the  $\beta$ 1-containing integrin.
6. The antagonist of claim 3 wherein the  $\beta$ 1-containing integrin is  $\alpha$ 5 $\beta$ 1 integrin.
7. The antagonist of claim 4 wherein the  $\beta$ 1-containing integrin is  $\alpha$ 5 $\beta$ 1 integrin.
8. The antagonist of claim 1 wherein the protein-protein interactions cause co-localization of the first protein and the second protein on a cell surface or a blood vessel.
9. The antagonist of claim 1 wherein said antagonist inhibits angiogenesis.
10. The antagonist of claim 1 wherein said antagonist inhibits tumor growth.
11. The antagonist of claim 1 wherein said antagonist inhibits metastasis.
12. The antagonist of claim 1 wherein said antagonist inhibits a disease state.
13. The antagonist of claim 12 wherein the disease is psoriasis, macular degeneration, a neurological disease, or restenosis in a tissue.

14. The antagonist of claim 1 wherein said antagonist is a monoclonal antibody.
15. The antagonist of claim 14 wherein said monoclonal antibody is monoclonal antibody FM155.
16. The antagonist of claim 1 wherein said antagonist has the binding specificity for at least one target of monoclonal antibody FM155.
17. The antagonist of claim 1 wherein the antagonist is a polyclonal antibody.
- ~~18.~~ The antagonist of claim 1 wherein the antagonist is a polypeptide, a linear peptide or a cyclic peptide.
- ~~19.~~ The antagonist of claim 1 wherein the antagonist is a non-peptidic compound.
- ~~20.~~ The antagonist of claim 1 wherein the antagonist is a small organic compound.
- ~~21.~~ The antagonist of claim 1 wherein the antagonist is an oligonucleotide.
22. The antagonist of claim 1 wherein the antagonist is a humanized or chemically modified monoclonal antibody.
23. The antagonist of claim 1 wherein the antagonist is a fragment of a monoclonal antibody.
24. The antagonist of claim 1 wherein the antagonist is conjugated to cytotoxic or cytostatic agents.
25. A polypeptide for inhibiting angiogenesis and/or tumor growth wherein the polypeptide specifically binds to MMP-9 with a binding affinity significantly greater than the binding capacity of SEQUENCE ID NO: 3 to MMP-9.
26. The polypeptide of claim 25 wherein the polypeptide is a protein.
27. The polypeptide of Claim 25 wherein the polypeptide has a sequence consisting of SEQUENCE ID NO: 1.

28. The polypeptide of Claim 25 wherein the amino acid sequence of the polypeptide comprises SEQUENCE ID NO: 1.
29. The polypeptide of Claim 25 wherein the polypeptide is a monoclonal antibody.
30. The polypeptide of Claim 29 wherein the monoclonal antibody is FM 155.
31. A polypeptide for inhibiting angiogenesis or tumor growth wherein the polypeptide specifically binds to a  $\beta$ 1 containing integrin with a binding affinity significantly greater than the binding affinity of SEQUENCE ID NO: 3 to the  $\beta$ 1 containing integrin.
32. The polypeptide of claim 31 wherein the polypeptide is a protein.
33. The polypeptide of Claim 31 wherein the polypeptide is SEQUENCE ID NO: 1.
34. The polypeptide of Claim 31 wherein the amino acid sequence of the polypeptide comprises SEQUENCE ID NO: 1.
35. The polypeptide of Claim 31 wherein the polypeptide is a monoclonal antibody.
36. The polypeptide of Claim 35 wherein the monoclonal antibody is FM 155.
37. An antagonist that specifically binds with SEQUENCE ID NO: 1 but binds to SEQUENCE ID NO: 3 with substantially reduced affinity.
38. The antagonist of claim 37 wherein the antagonist inhibits angiogenesis.
39. The antagonist of claim 37 wherein the antagonist inhibits tumor growth.
40. The antagonist of claim 37 wherein the antagonist is a polypeptide.
41. The polypeptide of claim 40 wherein the polypeptide is a protein.
42. The polypeptide of Claim 40 wherein the polypeptide comprises SEQUENCE ID NO: 1.
43. The polypeptide of Claim 40 wherein the polypeptide is a monoclonal antibody.

44. The polypeptide of Claim 43 wherein the monoclonal antibody is FM 155.
45. An antagonist that disrupts the localization of MMP-9 on a cell surface or blood vessel.
46. The antagonist of claim 45 wherein the antagonist inhibits angiogenesis.
47. The antagonist of claim 45 wherein the antagonist inhibits tumor growth.
48. The antagonist of claim 45 wherein the antagonist is a polypeptide.
49. The polypeptide of claim 48 wherein the polypeptide is a protein.
50. The polypeptide of Claim 48 wherein the polypeptide comprises SEQUENCE ID NO:1.
51. The polypeptide of Claim 48 wherein the polypeptide is a monoclonal antibody.
52. The polypeptide of Claim 51 wherein the monoclonal antibody is FM 155.
53. A method of inhibiting angiogenesis in a tissue comprising administering the antagonist of claim 1.
54. The method of claim 53 wherein said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.
55. The method of claim 53 wherein said antagonist is administered in conjunction with chemotherapy.
56. The method of claim 53 wherein said antagonist is administered in conjunction with radiation.
57. The method of claim 53 wherein the tissue is inflamed and angiogenesis is occurring.
58. The method of claim 57 wherein the tissue is present in a mammal.
59. The method of claim 58 wherein the tissue is arthritic, ocular, retinal or a hemangioma.

60. A method of inhibiting tumor growth or metastasis in a tissue comprising administering the antagonist of claim 1.
61. The method of claim 60 wherein said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, topically or orally.
62. The method of claim 60 wherein said antagonist is administered in conjunction with chemotherapy.
63. The method of claim 60 wherein said antagonist is administered in conjunction with radiation.
64. The method of claim 60 wherein the tumor or metastasis is a melanoma, carcinoma, sarcoma, fibrosarcoma, glioma or astrocytoma.
65. A method of inhibiting psoriasis, macular degeneration, or restenosis in a tissue by administering the antagonist of claim 1.
66. The method of claim 65 wherein said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.
67. The method of claim 65 wherein administering the antagonist is in conjunction with chemotherapy.
68. The method of claim 65 wherein administering the antagonist is in conjunction with radiation.
69. A method of detecting angiogenesis in a tissue by contacting the antagonist of claim 1 with said tissue.
70. The method of claim 69 wherein said tissue is *ex vivo*.

71. The method of claim 69 wherein said tissue is *in vivo* and said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.

72. The method of claim 69 wherein said antagonist is conjugated to a fluorochrome, radioactive tag, paramagnetic heavy metal, diagnostic dye or enzyme.

73. A method of detecting tumors or tumor invasion in a tissue by administering the antagonist of claim 1.

74. The method of claim 73 wherein said tissue is *ex vivo*.

75. The method of claim 73 wherein said tissue is *in vivo* and said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.

76. The method of claims 73 wherein said antagonist is conjugated to a fluorochrome, radioactive tag, paramagnetic heavy metal or diagnostic dye.

77. A method for screening for MMP-9 antagonists comprising:

- a) providing a putative antagonist;
- b) measuring said putative antagonist's first affinity for binding with MMP-9;
- c) measuring a second affinity of SEQUENCE ID NO: 3 for binding with MMP-9;
- d) selecting said putative antagonist as an MMP-9 antagonist if said second affinity is substantially less than said first affinity.

78. The method of claim 77 wherein said putative antagonist is a non-peptidic compound.

79. The method of claim 77 wherein said non-peptidic compound is a small organic compound. *constant*
80. The method of claim 78 wherein said non-peptidic compound is an oligonucleotide.
81. The method of claim 77 wherein said putative antagonist is a polypeptide, a linear peptide or a cyclic peptide.
82. The method of claim 77 wherein said putative antagonist is an antibody.
83. The method of claim 82 wherein said antibody is monoclonal.
84. The method of claim 82 wherein said antibody is polyclonal.
85. The method of claim 77 wherein said first and said second affinities are measured by an enzyme linked immunosorbent assay.
86. The method of claim 77 wherein said second affinity is about 3 times less than said first affinity.
87. The method of claim 77 wherein said second affinity is about 5 times less than said first affinity.
88. The method of claim 77 wherein said second affinity is about 10 times less than said first affinity.
89. A method for screening for  $\beta$ 1 integrin antagonists comprising:
- a) providing a putative antagonist;
  - b) measuring said putative antagonist's first affinity for binding with a  $\beta$ 1 integrin;
  - c) measuring a second affinity of SEQUENCE ID NO: 3 for binding with said  $\beta$ 1 integrin;

d) selecting said putative antagonist as a  $\beta 1$  integrin antagonist if said second affinity is substantially less than said first affinity.

90. The method of claim 89 wherein said putative antagonist is a non-peptidic compound.

91. The method of claim 89 wherein said non-peptidic compound is a small organic compound.

92. The method of claim 90 wherein said non-peptidic compound is an oligonucleotide.

93. The method of claim 89 wherein said putative antagonist is a polypeptide, a linear peptide or a cyclic peptide.

94. The method of claim 89 wherein said putative antagonist is an antibody.

95. The method of claim 93 wherein said antibody is monoclonal.

96. The method of claim 93 wherein said antibody is polyclonal.

97. The method of claim 89 wherein said first and said second affinities are measured by an enzyme linked immunosorbent assay.

98. The method of claim 89 wherein said second affinity is about 3 times less than said first affinity.

99. The method of claim 89 wherein said second affinity is about 5 times less than said first affinity.

100. The method of claim 89 wherein said second affinity is about 10 times less than said first affinity.

101. A peptide comprising a sequence encoding an epitope recognized by an antagonist of claim 1.

102. The peptide of claim 101 wherein said antagonist is a monoclonal antibody.



103. The peptide of claim 102 wherein said antibody is FM155.
104. The peptide of claim 101 wherein said peptide is SEQ ID NO: 1.

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